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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/030,985	02/26/98	FALO JR	L	214001-00648

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EXAMINER	
VANDER VEGT,F	
ART UNIT	**PAPER NUMBER**
1644	13

DATE MAILED: 02/17/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/030,985	Applicant(s) Falo et al
	Examiner F. Pierre VanderVegt	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Nov 29, 1999* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/~~are~~ pending in the application.

Of the above, claim(s) *1-12, 16, and 25-36* is/~~are~~ withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-15 and 17-24* is/~~are~~ rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This application claims priority to provisional application 60/039,472.

Claims 1-36 are currently pending in this application.

Claims 1-12 and 25-36 stand withdrawn as being drawn to a non-elected invention.

Claim 16 stands withdrawn as being drawn to a non-elected species.

Accordingly, **claims 13-15 and 17-24 are the subject of examination** in the present Office Action.

Election/Restriction

1. This application contains claims 1-12, 16 and 25-36, which are drawn to inventions non-elected with traverse in Paper No. 8, filed November 25, 1998. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) MPEP § 821.01.

2. In view of the amendment filed November 29, 1999, only the following rejections are maintained.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 13-14 and 17-24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Flamand et al (B on form PTO-1449) as evidenced by Unanue (U on form PTO-892) and Dezutter-Dambuyant (V).

It was previously stated: "The Flamand et al reference teaches the in vitro incubation of murine dendritic cells with tumor specific antigen from murine BCL1 lymphoma cells (Abstract in particular)[claims 13 and 17-19]. While Flamand et al teaches only the use of splenic antigen

presenting cells, Unanue provides evidence that splenic dendritic cells are the same as those found in lymph nodes and as the Langerhans cells of the skin (page 102, subsection "General Characteristics" in particular) and Dezutter-Dambuyant evidences that these are also the same as the dermal dendritic cells and which arise from bone marrow precursors (Abstract in particular)[claim 14]. Flamand et al further teaches that a product of this in vitro incubation, or pulsing, is dendritic cells which are "loaded" with idiotype protein specific to the BCL1 lymphoma cells (page 605, last paragraph of "Introduction" in particular). Flamand et al also teaches the formulation of these cells as a pharmaceutical preparation which can be administered to mice prophylactically to protect them from a challenge with a normally lethal dose of BCL1 lymphoma cells (page 606, section "*In vivo* treatment" and page 605, last paragraph of "Introduction" in particular)[claims 20-24]. Flamand et al also teaches the products of co-incubating B cells with antigen (page 606, sections "Antigen-presenting cells" and "*In vivo* treatment" in particular)[claim 13]. While Flamand et al does not teach Applicant's method of the co-incubation of antigen presenting cells with tumor cells, Applicant claims are drawn not to the method, but rather to the "products of co-cultures," in other words, the instant claims are product-by-process claims. Applicant's disclosed method and the method of Flamand et al both result in the generation of the same product, dendritic cells which are loaded with tumor-specific antigen which can present antigenic fragments to T cells for the purpose of activating a tumor-specific immune response. Applicant is reminded that a product remains the same irrespective of the manner in which it is produced. Claims 17-19 and 22-24 are included because the ratio of cells used in Applicant's method of manufacturing the product would not change the basic nature of the claimed product, only the ratio of loaded to non-loaded dendritic cells and/or the amount of tumor-specific antigen loaded onto each individual dendritic cell and the claims are not drawn to the ratio of product or expression level. The prior art teaching anticipates the claimed invention."

Applicant's arguments filed November 29, 1999 have been fully considered but they are not persuasive.

Applicant contends that the Flamand et al reference does not apply because Flamand et al does not teach co-culture of at least two cell types, rather the culture of dendritic cells with a specific antigen to generate dendritic cells presenting that antigen alone. Applicant argues that this could not be anticipatory because Flamand et al does not teach all of the products of the co-culture of two cell types. The Examiner respectfully disagrees with Applicant's position regarding the scope of the claimed invention versus the teachings of Flamand et al. While it is acknowledged that Applicant's disclosure in the instant specification encompasses, as the products of co-culture, more than just dendritic cells programmed to present a single antigen, Applicant is reminded that the claims are to be given the broadest reasonable interpretation based upon the language of the claim and, while claims are to be read in light of the specification,

limitations of the specification are not to be read into the claims. The claims are broadly drawn to formulations comprising the products of co-culture, without limitation to any specific products of said co-culture. One of ordinary skill in the art at the time the invention was made would have known that said products would include dendritic cells which bear on their surface antigenic fragments of single antigens derived from the target cells, thereby becoming programmed to present these antigenic fragments to T cells and capable of activating T cell reactivity to these single antigens derived from the target cells. While utilizing a different method, the Flamand et al reference teaches dendritic cells programmed to present antigenic fragments of tumor antigens to T cells to stimulate an immune response to the tumor which the antigen is derived from. Accordingly, the teachings of Flamand et al are commensurate in scope with the language of the claims and are anticipatory of the claimed formulation.

4. Claims 13-15 and 17-24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Mayordomo et al (D on form PTO-1449) as evidenced by Unanue (U on form PTO-892) and Dezutter-Dambuyant (V).

It was previously stated: "The Mayordomo et al reference teaches the incubation of dendritic cells with tumor specific antigens from lung carcinoma, sarcoma and melanoma cell lines (page 1298, paragraph bridging columns in particular). Mayordomo et al further teaches that a product of this in vitro incubation, or tumor peptide pulsing, is dendritic cells which are "loaded" with tumor specific antigens [claims 13, 15]. While Mayordomo et al teaches only the use of bone marrow derived dendritic cells and Langerhans cells (page 1301, paragraph bridging columns in particular), Unanue provides evidence that splenic dendritic cells are the same as those found in lymph nodes and as the Langerhans cells of the skin (page 102, subsection "General Characteristics" in particular) and Dezutter-Dambuyant evidences that these are also the same as the dermal dendritic cells and which arise from bone marrow precursors (Abstract in particular)[claim 14]. Mayordomo et al also teaches pharmaceutical preparations which are suitable as a vaccine which can be administered to mice prophylactically to protect them from a challenge of the specific tumor in all three models (page 1298, section "Dendritic cell-presenting tumour peptides as vaccines" and Figure 1 in particular) and that these tumor peptide-pulsed dendritic cells induce highly specific cytotoxic T lymphocytes in vivo (pages 1298-1299, section "Tumour peptide-pulsed dendritic cells induce CTLs *in vivo*" in particular)[claims 20-24]. While Mayordomo et al does not teach Applicant's method of the co-incubation of antigen presenting cells with tumor cells, Applicant claims are drawn not to the method, but rather to the "products of co-cultures," in other words, the instant claims are product-by-process claims. Applicant's

disclosed method and the method of Mayordomo et al both result in the generation of the same product, dendritic cells which are loaded with tumor-specific antigen which can present antigenic fragments to T cells for the purpose of activating a tumor-specific immune response. Applicant is reminded that a product remains the same irrespective of the manner in which it is produced. Claims 17-19 and 22-24 are included because the ratio of cells used in Applicant's method of manufacturing the product would not change the basic nature of the claimed product, only the ratio of loaded to non-loaded dendritic cells and/or the amount of tumor-specific antigen loaded onto each individual dendritic cell and the claims are not drawn to the ratio of product or expression level. The prior art teaching anticipates the claimed invention."

Similar to the argument addressed supra, Applicant contends that the Mayordomo et al reference does not apply because Mayordomo et al does not teach co-culture of at least two cell types, rather the culture of dendritic cells with a specific antigen to generate dendritic cells presenting that antigen alone. Applicant argues that this could not be anticipatory because Mayordomo et al does not teach all of the products of the co-culture of two cell types. The Examiner respectfully disagrees with Applicant's position regarding the scope of the claimed invention versus the teachings of Mayordomo et al. While it is acknowledged that Applicant's disclosure in the instant specification encompasses, as the products of co-culture, more than just dendritic cells programmed to present a single antigen, Applicant is reminded that the claims are to be given the broadest reasonable interpretation based upon the language of the claim and, while claims are to be read in light of the specification, limitations of the specification are not to be read into the claims. The claims are broadly drawn to formulations comprising the products of co-culture, without limitation to any specific products of said co-culture. One of ordinary skill in the art at the time the invention was made would have known that said products would include dendritic cells which bear on their surface antigenic fragments of single antigens derived from the target cells, thereby becoming programmed to present these antigenic fragments to T cells and capable of activating T cell reactivity to these single antigens derived from the target cells. While utilizing a different method, the Mayordomo et al reference teaches dendritic cells programmed to present antigenic fragments of tumor antigens to T cells to stimulate an immune response to the tumor which the antigen is derived from. Accordingly, the teachings of Mayordomo et al are commensurate in scope with the language of the claims and are anticipatory of the claimed formulation.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2000 366-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
February 14, 2000

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
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